44

Claims:

1. A compound of formula (II), or a pharmaceutically or veterinarily acceptable salt, hydrate or solvate thereof

$$Q \xrightarrow{R_1} O \xrightarrow{R_3} \overset{R_4}{N} Y \xrightarrow{A} N \xrightarrow{R_5} (II)$$

wherein

Q represents a radical of formula -N(OH)CH(=O) or formula -C(=O)NH(OH);

 R_1 represents hydrogen, methyl or trifluoromethyl, or, except when Z is a radical of formula -N(OH)CH(=O), a hydroxy, halo or amino group;

R₂ represents a group R₁₀-(V)₀-(ALK)_m- wherein

 R_{10} represents hydrogen, or a C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, cycloalkyl, aryl, or heterocyclyl group, any of which may be unsubstituted or substituted by $(C_1$ - C_6)alkyl, $(C_1$ - C_6)alkoxy, hydroxy, mercapto, $(C_1$ - C_6)alkylthio, amino, halo (including fluoro, chloro, bromo and iodo), trifluoromethyl, cyano, nitro, oxo, -COOH, -CONH $_2$, -COOR A , -NHCOR A , -CONH A , -NHR A , -NR A R B , or -CONR A R B wherein R A and R B are independently a $(C_1$ - C_6)alkyl group and

ALK represents a straight or branched divalent C_1 - C_6 alkylene, C_2 - C_6 alkynylene radical, and may be interrupted by one or more non-adjacent -NH-, -O- or -S- linkages,

V represents -NH-, -O- or -S-, and

m and n are independently 0 or 1;

R₃ represents the side chain of a natural or non-natural alpha amino acid;

R₄ represents hydrogen or C₁-C₃ alkyl;

Y represents N or CH;

ring A is optionally substituted on one or more ring carbon atoms by C_1 - C_3 alkyl, C_1 - C_3 alkoxy, or halo; and

R₅ represents a group (IIA),

$$\rightarrow$$
 (IIA)

wherein

m is 0 or 1;

Alk¹ represents a divalent C₁-C₃ alkylene radical;

Z represents hydrogen or cycloalkyl, phenyl or heterocyclic which is optionally substituted by

 (C_1-C_6) alkyl,

phenyl

monocyclic 5 or 6-membered heterocyclic,

benzyl,

phenoxy, or (C₁-C₆)alkoxy,

phenylthio or (C₁-C₆)alkylthio, any of which is in turn optionally substituted by:

hydroxy or mercapto,

trifluoromethyl,

oxo,

nitro,

cyano (-CN)
bromo, chloro, fluoro, or iodo
-COOH, or -COOR^A,
-CONH₂, -CONHR^A, or -CONR^AR^B
-COR^A, -SO₂R^A,
-NHCOR^A,
-NH₂, -NHR^A, or -NR^AR^B,
wherein R^A and R^B are independently a (C₁-C₆) alkyl
group, or R^A and R^B taken together with the
nitrogen atom to which they are attached form a 5or 6-membered heterocyclic ring which may
besubstituted by (C₁C₃)alkyl, hydroxy, or

2. A compound as claimed in claim 1 wherein Z represents cycloalkyl, phenyl or monocyclic-heterocyclic, which is optionally substituted by

hydroxy(C₁-C₃)alkyl.

(C₁-C₆)alkyl, (C₂-C₆)alkenyl, or (C₂-C₆)alkynyl, phenyl, or halophenyl, trifluoromethyl, monocyclic 5 or 6-membered hetrocyclic, benzyl, or halophenylmethyl, hydroxy, phenoxy, (C₁-C₆)alkoxy, or hydroxy(C₁-C₆)alkyl, mercapto, (C₁-C₆)alkylthio or mercapto(C₁-C₆)alkyl, oxo, nitro, cyano (-CN) bromo, chloro, fluoro, or iodo -COOH, or -COOR^A, -CONH₂, -CONHR^A, or -CONR^AR^B -COR^A, -SO₂R^A, -NHCOR^A,

-NH₂, -NHR^A, or -NR^AR^B,

wherein R^A and R^B are independently a (C_1-C_6) alkyl group, or R^A and R^B taken together with the nitrogen atom to which they are attached form a 5- or 6-membered heterocyclic ring which may be substituted by (C_1C_3) alkyl, hydroxy, or hydroxy (C_1-C_3) alkyl.

- 3. A compound as claimed in claim 1or claim 2 wherein R_1 is hydrogen.
- 4. A compound as claimed in any of the preceding claims wherein R_2 is (C_1-C_6) alkyl-, cycloalkyl (C_1-C_6) alkyl-, (C_1-C_3) alkyl-S- (C_1-C_3) alkyl-, or (C_1-C_3) alkyl-.
- 5. A compound as claimed in any of claims 1 to 3 wherein R₂ is n-propyl, n-butyl, n-pentyl, cyclopentylmethyl, cyclopentylethyl, cyclohexylmethyl or cyclohexylethyl.
- 6. A compound as claimed in any of the preceding claims wherein R₃ is

the characterising group of a natural α amino acid, for example benzyl, or 4-methoxyphenylmethyl, in which any functional group may be protected, any amino group may be acylated and any carboxyl group present may be amidated; or

a group - $[Alk]_nR_9$ where Alk is a (C_1-C_6) alkylene or (C_2-C_6) alkenylene group optionally interrupted by one or more -O-, or -S- atoms or -N(R_{12})- groups [where R_{12} is a hydrogen atom or a (C_1-C_6) alkyl group], n is 0 or 1, and R_9 is hydrogen or an optionally substituted phenyl, aryl, heterocyclyl, cycloalkyl or cycloalkenyl group or (only when n is 1) R_9 may additionally be hydroxy, mercapto, (C_1-C_8) alkylthio, amino, halo, trifluoromethyl, nitro, -COOH, -

CONH₂, -COOR^A, -NHCOR^A, -CONHR^A, -NHR^A, -NR^AR^B, or -CONR^AR^B wherein R^A and R^B are independently a (C₁-C₆)alkyl group; or

a benzyl group substituted in the phenyl ring by a group of formula - OCH_2COR_8 where R_8 is hydroxyl, amino, (C_1-C_6) alkoxy, phenyl (C_1-C_6) alkylamino, di $((C_1-C_6)$ alkylamino, phenyl (C_1-C_6) alkylamino; or

a heterocyclic(C_1 - C_6)alkyl group, either being unsubstituted or mono- or disubstituted in the heterocyclic ring with halo, nitro, carboxy, (C_1 - C_6)alkoxy, cyano, (C_1 - C_6)alkanoyl, trifluoromethyl (C_1 - C_6)alkyl, hydroxy, formyl, amino, (C_1 - C_6)alkylamino, di-(C_1 - C_6)alkylamino, mercapto, (C_1 - C_6)alkylthio, hydroxy(C_1 - C_6)alkyl, mercapto(C_1 - C_6)alkyl or (C_1 - C_6)alkylphenylmethyl; or

a group -CR_aR_bR_c in which:

each of R_a , R_b and R_c is independently hydrogen, (C_1-C_6) alkyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, phenyl (C_1-C_6) alkyl, (C_3-C_8) cycloalkyl; or

 R_c is hydrogen and R_a and R_b are independently phenyl or heteroaryl such as pyridyl; or

 R_c is hydrogen, (C_1-C_6) alkyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, phenyl (C_1-C_6) alkyl, or (C_3-C_8) cycloalkyl, and R_a and R_b together with the carbon atom to which they are attached form a 3 to 8 membered cycloalkyl or a 5- to 6-membered heterocyclic ring; or

R_a, R_b and R_c together with the carbon atom to which they are attached form a tricyclic ring (for example adamantyl); or

 R_a and R_b are each independently (C_1 - C_6)alkyl, (C_2 - C_6)alkenyl, (C_2 - C_6)alkynyl, phenyl(C_1 - C_6)alkyl, or a group as defined for R_c below other than hydrogen, or R_a and R_b together with the carbon atom to which

they are attached form a cycloalkyl or heterocyclic ring, and R_c is hydrogen, -OH, -SH, halogen, -CN, -CO $_2$ H, (C $_1$ -C $_4$)perfluoroalkyl, -CH $_2$ OH, -CO $_2$ (C $_1$ -C $_6$)alkyl, -O(C $_1$ -C $_6$)alkyl, -O(C $_2$ -C $_6$)alkenyl, -S(C $_1$ -C $_6$)alkyl, -SO(C $_1$ -C $_6$)alkyl, -SO(C $_1$ -C $_6$)alkyl, -SO(C $_2$ -C $_6$)alkenyl, -SO $_2$ (C $_2$ -C $_6$)alkenyl or a group -Q-W wherein Q represents a bond or -O-, -S-, -SO- or -SO $_2$ - and W represents a phenyl, phenylalkyl, (C $_3$ -C $_8$)cycloalkyl, (C $_3$ -C $_8$)cycloalkyl, (C $_3$ -C $_8$)cycloalkenylalkyl, heteroaryl or heteroarylalkyl group, which group W may optionally be substituted by one or more substituents independently selected from, hydroxyl, halogen, -CN, -CO $_2$ H, -CO $_2$ (C $_1$ -C $_6$)alkyl, -CONH $_2$, -CONH(C $_1$ -C $_6$)alkyl, -CHO, -CH $_2$ OH, (C $_1$ -C $_6$)alkyl, -O(C $_1$ -C $_6$)alkyl, -SO(C $_1$ -C $_6$)alkyl, (C $_2$ -C $_6$)alkyl, (C $_3$ -C

- 7. A compound as claimed in any of claims 1 to 6 wherein R₃ is methyl, ethyl, n-propyl, n-butyl, benzyl, 4-chlorobenzyl, 4-hydroxybenzyl, phenyl, cyclohexyl, cyclohexylmethyl, pyridin-3-ylmethyl, tert-butoxymethyl, naphthylmethyl, iso-butyl, sec-butyl, tert-butyl, 1-benzylthio-1-methylethyl, 1-methylthio-1-methylethyl, 1-methylethyl, 1-methylethyl, 1-hydroxy-1-methylethyl, 1-fluoro-1-methylethyl, hydroxymethyl, 2-hydroxethyl, 2-carboxyethyl, 2-methylcarbamoylethyl, 2-carbamoylethyl, or 4-aminobutyl.
- 8. A compound as claimed in any of claims 1 to 6 wherein R_3 is tert-butyl, isobutyl, benzyl, isopropyl or methyl.
- 9. A compound as claimed in any of the preceding claims wherein R_{λ} is methyl.
- 10. A compound, method, use or composition as claimed in any of the preceding claims wherein in the group R_5 , m is 1, and Alk^1 is $-(CH_2)$ or $-(CH_2CH_2)$ -.

- 11. A compound as claimed in any of the preceding claims wherein, in the group R_5 , Z is a phenyl,pyridyl, thienyl, furanyl, pyranyl, pyrolyl, diazolyl, triazolyl, thiazolyl, thiadiazolyl, oxazolyl, ozadiazolyl, indolyl, benzisozazolyl, benzthiazolyl or imidazothiazolyl ring, optionally substituted as specified in claim 1 of claim 2.
- 12. A compound as claimed in claim 11 wherein the ring Z is unsubstituted or substituted by methyl, methoxy, ethoxy, methoxymethyl, ethylthio, chloro, bromo, hydroxy, nitro, phenyl, 2- or 4-nitrophenyl, dimethylamino, dimethylaminophenyl, methylsulphonyl, dimethylaminosulphonyl, 3-pyridyl or 2-pyrazin-2-yl.
- 12. A compound as claimed in any of claims 1 to 10 wherein, in the group R_5 , Z is a cyclopentyl, cyclohexyl, phenyl, morpholinyl, pyrimidin-2-yl, 1,2,3-thiadiazol-5-yl, 1,4-thiazol-5-yl, benzofuran-2-yl, 2-or 3-furanyl, 2- or 3-thienyl, 2- or 3-pyranyl, 2-, 3- or 4-pyrrolyl, 3-, 4- or 5-pyrazolyl, 3-, 4- or 5-isoxazolyl, or 2-, 3- or 4-pyridyl ring any of which may optionally be substituted by hydroxy, methoxy, ethoxy, mercapto, methylthio, ethylthio, methyl, ethyl, trfluoromethyl, fluoro, chloro, amino, methylamino, or dimethylamino.
- 13. A compound as claimed in claim 1or claim 2 wherein the compound is one specifically named and/or exemplified herein, or is the hydroxamate (Q represents a radical of formula -C(=O)NH(OH)) analogue thereof.
- 14. A method for the treatment of bacterial infections in humans and non-human mammals, which comprises administering to a subject suffering such infection an antibacterially effective dose of a compound as claimed in any of claims 1 to 13.
- 15. A method for the treatment of bacterial contamination by applying an antibacterially effective amount of a compound as claimed in any of claims 1 to 13to the site of contamination.

WO 03/089412 PCT/GB03/01541

51

- 16. The use of a compound as claimed in any of claims 1 to 13 in the manufacture of an antibacterial composition.
- 17. A pharmaceutical or veterinary composition comprising a compound as claimed in any of claims 1 to 13together with a pharmaceutically of veterinarily acceptable carrier.